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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/820,416	03/29/2001	David Bar-Or	4172-15-1	5597

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EXAMINER
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ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/12/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/820,416	BAR-OR ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/13/2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-68* is/are pending in the application.

4a) Of the above claim(s) *54,55,59,62and 65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-53,56-58,60,61,63,64 and 66-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14,17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment B, received November 13, 2002, paper 16 is acknowledged. Claims 69-101 were canceled. Claim 48 was amended. Priority statement on first page of the specification was amended.

2. Currently claims 48-68 are pending

3. Claims 54-55, 59, 62 and 65 are withdrawn from further consideration pursuant to37 CFR 1.142(b), as being drawn to non-elected inventions.

4. Claims 48, 49, 50-53, 56-58, 60-61, 63-64 and 66- 68 are under consideration.

Prior Citations of Title 35 Sections

5. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Prior Citations of References

6. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No form PTO-892 has been submitted with this office action.

Information Disclosure Statement

7. Information disclosure statements, received, September 9, 2002 and November 13, 2002 papers 14 and 17 are acknowledged. No copies of the references were submitted. Applicants referred to the priority application Serial No. 09/165,961 for those documents. The examiner has located the references and has considered the references (see attached 1449 forms).

Election/Restrictions

8. Applicants' argue that claims 54-55, 59, 62 and 65 should not have been withdrawn from further consideration as being drawn to non-elected inventions because those claims are within elected Group I (claims 48-68).

Applicants' arguments filed November 13, 2002 have been fully considered but they are not persuasive.

It is the examiner's position that applicants elected, with out traverse, species "produce" from claim 48, superoxide dismutase from claim 50, serum from claim 53 cobalt from claims 57 and 68 and atomic absorption from claim 58. Claims 54-55, 59, 62 and 65 , are withdrawn from further consideration pursuant to37 CFR 1.142(b), as being drawn to Non-elected species.

Objections Withdrawn

9. Objection to the priority statement made in paragraph 7 of the office action mailed July 02, 2002, paper # 13 is withdrawn in view of applicant's amendments.

Rejections Withdrawn

10. Rejection of claims 48, 49, 50-53, 56-58, 60-61, 63-64 and 66- 68 under 35 U.S.C. 112, second paragraph made in paragraph 8 of the office action mailed July 02, 2002, paper # 13 is withdrawn in view of applicant's amendments.

Rejections Maintained

11. Rejection of claims 48, 49, 50-53, 56-58, 60-61, 63-64 and 66- 68 under 35 103 (a) made in paragraph 9 of the office action mailed July 02, 2002, paper # 13 is maintained.

The rejection was as stated below:

Claims 48, 49, 50-53, 56-58, 60-61, 63-64 and 66- 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bar-Or et al. (US Patent No: 5,227,307) in view of Crapo et al. (US Patent No. 5,994,339) and further in view of Young et al. (6,375,930).

Claims are drawn to a method of monitoring or assessing treatment of a disease or condition with a compound that produces free radicals comprising:

a) obtaining a biological sample;

b) treating the patient with a compound;

c) obtaining additional biological samples after treatment; and determining the change of albumin in the sample by:

d) contacting each of the biological sample with excess quantity of a metal ion salt;

e) determing the amount of bound metal ion to the albumin;

f) determing if there is a change in the amount of bound metal ion.

Bar-Or et al. (US Patent No: 5,227,307) teach a method of monitoring disease or condition in a patient that produces free radicals comprising:

a) obtaining a biological sample and determining the change of albumin in the sample by:

b) contacting each of the biological sample with excess quantity of a metal ion salt;

c) determing the amount of bound metal ion to the albumin;

d) determing if there is a change in the amount of bound metal ion.

(see abstract and claims).

Bar-Or et al. teach a method for detecting ischemic states (lack of oxygen) in a patient by contacting a sample of serum with a metal ion capable of binding to metal binding sites in the sample to form a mixture and then detecting the presence of unbound metal ion to determine the ischemic event (see example 1 and claims). Furthermore, the prior art teaches that several methods could be used to measure the metal ion binding to the albumin such as atomic absorption, atomic emission spectroscopy and determing the color intensity by spectrophotometer (see column 3, lines 44-54). Bar-Or et al. teach a variety of metal ion salts including cobalt (see column 5, lines 23-40). Bar-Or et al. teach that the quantity of free metal ions in the sample may also be detected by colorimetric means and teach a variety of color forming compounds (see column 6, lines 20-65). Bar-Or et al. (US Patent No: 5,290,519) teach a method of quantifying modified albumin, column 3, lines 14-22 recite that " In the present method, a sample of serum, plasma, fluid or tissue from a patient is reached with metal ions, generally in the form of an aqueous salt solution, so that the metal ion become bound to the metal binding sites on the protein in the sample. Metal ions bind to the proteins containing metal ion- binding sites such as thiol, hydroxy, carboxy, amino groups present on the amino acids which constitute the protein." Therefore, Bar-Or et al. teach modified protein (i.e. modified albumin) since metal binding capacity is reduced or inhibited in the albumin. Bar-Or et al. do not teach treating patient with a compound or superoxide dismutase as a free radical scavenger. However, Crapo et al. teach treating patient with an effective amount of a mimetic of superoxide dismutase as a free radical scavenger (see column 1, background, column 2, summary of invention and claims specially claim 1). Crapo et al. do not teach photosensitizing agents and porfimer sodium. However, Young et al. teach photodynamic therapy and porfimer sodium (see

column 3, lines 10-20 and column 4, lines 50-56). It would have *prima facie* obvious to a person of ordinary skill in art at the time the invention was made to use and combine the methods set forth in Bar-Or et al., Crapo et al. and Young et al. to obtain the claimed invention. One of ordinary skill in art would have been motivated with the reasonable expectation of success to develop a method of monitoring or assessing treatment of a disease by detecting or quantifying free radical damage as taught by Bar-Or et al. absent any convincing evidence to the contrary.

Applicants' arguments filed November 13, 2002 have been fully considered but they are not persuasive.

Applicants argue that Bar-Or et al. do not teach or suggest monitoring or assessing the effectiveness of treatment of patients with drugs that produce or reduce free radicals. Applicants further argue that Crapo et al. and Young et al. do teach the treatment of diseases with oxidant scavengers. Applicants further argue, there is no basis for combining the teachings of cited references, and it is submitted that the Examiner has improperly reconstructed the invention through hindsight.

It is the examiner's position that Bar-Or et al. teach or suggest monitoring or assessing the effectiveness of treatment of patients for example in column 2, lines 23-25 Bar-Or et al. recite " A further object of the invention is to provide a method for evaluating rehabilitated patients suffering from ischemia (myocardial infraction) to determine circulatory effectiveness", in column 9 lines 34-41 Bar-Or et al. recite " The results indicate that the present method can be used to detect ischemic states. The present method is effective in distinguishing between ischemic cardiogenic chest pain and non-cardiogenic chest pain. Obviously, numerous modifications and variations of the present invention are possible in light of the above teachings.

It is therefore to be understood that within the scope of the appended claims, the invention may be practiced other than as specifically described herein".

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Bar-Or et al. suggest the motivation to combine the references for example see column 9 lines 34-41 which recite "Obviously, numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced other than as specifically described herein".

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

12. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from 7:30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

February 25, 2003

LYNETTE R. F. SMITH
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